FreeStyle Navigator®

Continuous Glucose Monitoring System

User's Guide

℞ Only

CAUTION: Federal law restricts this device to sale by or on the order of a physician.

Abbott

Indications for Use

The FreeStyle Navigator® Continuous Glucose Monitoring System is indicated for continually recording interstitial fluid glucose levels in people (ages 18 and older) with diabetes mellitus for the purpose of improving diabetes management. Readings and alarms about glucose levels from FreeStyle Navigator® Continuous Glucose Monitoring System are not intended to replace traditional blood glucose monitoring. Before adjusting therapy for diabetes management based on the results and alarms from the FreeStyle Navigator® Continuous Glucose Monitoring System, traditional blood glucose tests must be performed. The FreeStyle Navigator® Continuous Glucose Monitoring System provides a built-in blood glucose meter to confirm the continuous glucose result.

The FreeStyle Navigator® Continuous Glucose Monitoring System provides real-time readings, graphs, trends, and glucose alarms directly to the user. The FreeStyle Navigator® Continuous Glucose Monitoring System is intended to be used in home settings to aid people with diabetes in predicting and detecting episodes of hypoglycemia and hyperglycemia and in clinical settings to aid health care professionals in evaluating glucose control. The FreeStyle Navigator® Continuous Glucose Monitoring System is available only by prescription.

Contraindications

The FreeStyle Navigator® Continuous Glucose Monitoring System must be removed prior to Magnetic Resonance Imaging (MRI).

Section 1 – Key Terms

- Alarms
- Blood Glucose Mode
- Continuous Monitoring Mode
- Freestyle Navigator Continuous Glucose Monitoring System
- Freestyle Test Strips
- *in vitro*
- Interstitial Fluid
- LEFT/RIGHT Option Buttons
- Receiver
- Receiver Display Screen
- Receiver Test Strip Port
- Reports
- Sensor
- Sensor Delivery Unit
- Sensor Inserter
- Sensor Insertion Button
- Sensor Locking Pin
- Sensor Release Tabs
- Sensor Support Mount
- Transmitter
- Transmitter Tabs
- UP/DOWN Arrow Buttons

1 Getting Acquainted

Introduction

Important: *Read all of the instructions in this User's Guide before using your FreeStyle Navigator® Continuous Glucose Monitoring System. Adjustments to your treatment should be done under the guidance of your healthcare team.*

Your FreeStyle Navigator system continuously reads, displays, and records the glucose levels in the fluids found between the cells under your skin (interstitial fluids). It does this by using a small, thin, plastic sensor inserted just under the skin.

Your FreeStyle Navigator system provides you with continuous glucose readings in real time. By having access to more frequent glucose measurements, you can monitor your glucose levels and gain an understanding of patterns in your glucose levels. This will help you and your healthcare team see how factors such as your diet, insulin, exercise, and diabetes medication affect your glucose levels, and to adjust your treatment plan accordingly.

Your FreeStyle Navigator system has a number of helpful features.

- Wireless communication between the transmitter and receiver.
- Disposable sensor that can be worn up to 5 days.
- Alarms to alert you to low or high glucose levels (hypoglycemia or hyperglycemia) ***before*** reaching those low and high glucose levels and when reaching those glucose levels.
- Graphs and statistics that show your glucose in easy-to-understand formats.
- Directional glucose trend arrows that show if your glucose values are rising or falling and how fast.
- Memory to hold up to 60 days worth of data.
- Wireless communication capabilities to a personal computer.
- Built-in FreeStyle® Blood Glucose Meter for performing blood glucose measurements.
- Event entry capabilities (like meals, exercise, insulin and other).
- Backlit display.

Important: *Keep this User's Guide for future reference. It will come in handy when you have to do procedures that you do not do often enough to remember.*

How are the parts packaged?

Your FreeStyle Navigator system comes with two kits:

- A System kit.
- A Sensor kit.

The System Kit

- *1 FreeStyle Navigator Receiver*
- *2 AAA Alkaline Batteries (for the receiver)*
- *1 FreeStyle Navigator Transmitter*
- *1 Silver Oxide 357 HC Battery (for the transmitter)*
- *1 Belt Clip (for the receiver)*
- *1 FreeStyle Lancing Device*
- *1 Finger Cap (for the lancing device)*
- *1 User's Guide*
- *1 Getting Started Guide*
- *1 Quick Reference Card*
- *1 Welcome Card*
- *6 Overbandages*
- *6 Alcohol Prep Pads*
- *6 IV wipes*
- *30 Sterile Lancets*
- *1 Vial of FreeStyle Control Solution and Insert*
- *1 Vial of 50 FreeStyle Strips and Strip Insert*
- *1 Warranty Registration Card*

The Sensor Kit

- *6 Sterile Sensor Delivery Units (each containing a sensor) and Product Insert*
- *1 Silver Oxide 357 HC Replacement Battery (for the transmitter)*

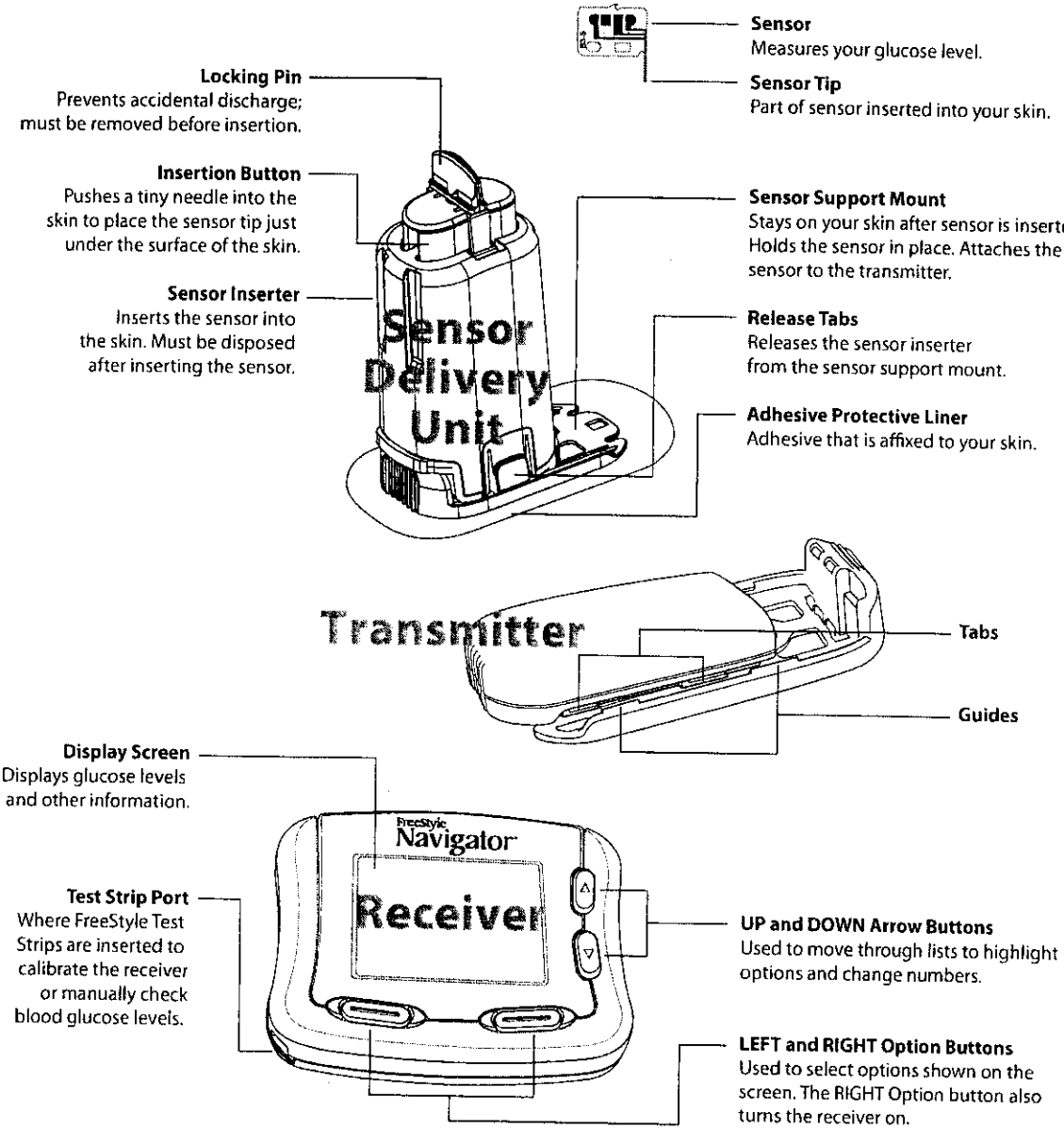
- In addition, FreeStyle Navigator system can transfer data to a computer wirelessly using Bluetooth® technology.

Important Notes:

- The FreeStyle Navigator® Continuous Glucose Monitoring System is designed as a complete system. Use only the FreeStyle Navigator Sensor, the FreeStyle Navigator Transmitter, the FreeStyle Navigator Receiver and FreeStyle Test Strips.
- The system is intended for your personal use; do **NOT** share your system with others.

What are the key parts of my system?

Your FreeStyle Navigator system includes the following major parts:



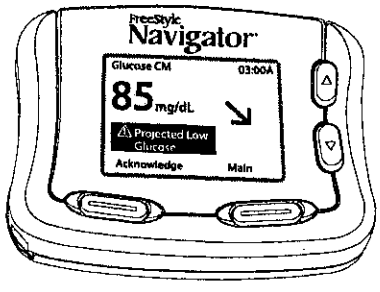
a. A FreeStyle Navigator Sensor that you insert about 5 mm under your skin. Each inserted sensor is intended to remain in place and provide a continuous glucose reading for up to 5 days. The sensor is contained in the Sensor Delivery Unit.

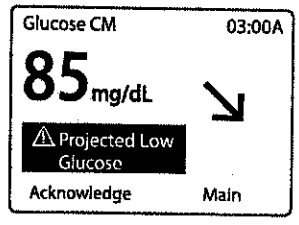
b. A wireless FreeStyle Navigator Transmitter (Tx), a small electronic device that connects to the sensor and sends glucose values to the receiver once every minute.

c. A wireless FreeStyle Navigator Receiver (Rx) that captures and displays glucose measurements. With the press of a button, the receiver displays the glucose measurement taken from the sensor.

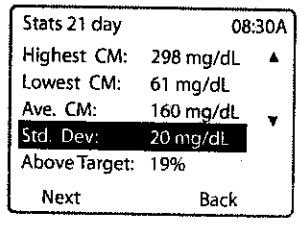
Note: The receiver also has a built-in FreeStyle Blood Glucose Meter that can be used for blood glucose testing. The receiver should always be kept with you on a belt, in a pocket, or in a purse.

Key features of the System

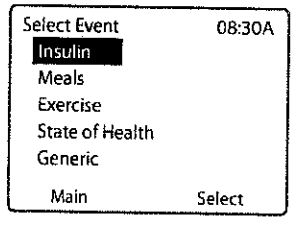




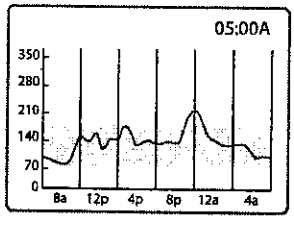
Alarms



Statistics



Event Log



Line Graph

Your receiver comes with backlight capability to see the screen in dark environments. The backlight can be turned on by pressing and releasing the DOWN Arrow button and then pressing and releasing the RIGHT Option button.

For more details on the different symbols and icons on the screen, see Section 9 on "Daily Use".

Using your system

For Daily Activities

You will be wearing a sensor and a transmitter at all times while you are using the system. Keep the following in mind as you go about your normal routine.

- Only wear the sensor and transmitter on a flat surface of either your abdomen or the back of your upper arm.
- ***Sleeping*** – The sensor and transmitter should not interfere with your normal sleeping patterns. As you get ready to go to sleep, place the receiver within 10 feet to maintain the transmitter-to-receiver connection.
- ***Bathing*** – Do **NOT** wear the receiver while bathing or showering. Do **NOT** allow the receiver to get wet. However, you can wear the sensor and transmitter while bathing or showering.
- ***Swimming*** – You may swim while wearing the sensor and transmitter. Do **NOT** go deeper than 1 meter (approximately 3 feet).

Note: The connection between the transmitter and receiver is **NOT** maintained when the transmitter is underwater; thus, you will **NOT** receive continuous glucose readings. However, when you take the sensor and transmitter out of the water, the continuous glucose readings will resume.

When Traveling by Plane

Note: Do **NOT** perform the upload data feature when you are on a commercial aircraft.

Follow the guidelines below when traveling. Always check with local authorities prior to departure as rules and regulations may change without notice.

At the airport:
Notify the security personnel of the presence of the device when going through the security systems.

On the plane:
Check with your airline before departure whether the device will be permitted aboard the aircraft. The airline companies set policy regarding the use of medical devices on board their flights.

If you want to disable the transmit function of the transmitter, follow these steps:

1. If you are currently wearing a sensor, remove the sensor.
2. Detach the transmitter from the sensor support mount and remove the battery from the transmitter.
3. Program into the receiver that you have ended a sensor session.
4. By removing the batteries from the transmitter, you have broken the connection between the transmitter and receiver. You can set the data loss alarms and system alarms to a short vibration mode in order to prevent the device from sounding alarms. Once you put a new battery into the transmitter, make sure to set the alarms to the original setting.

Note: Insert a fresh battery into the transmitter after travel before inserting a new sensor.

You can always use your receiver to check your blood glucose manually in the Blood Glucose mode.

How do I prepare my system for the first time?

When you are setting up your receiver for the first time, perform all of the procedures listed below ***in the order that they are listed.*** Check each procedure off when you complete it.

- ❑ Install batteries in the transmitter first and then in the receiver (*see Section 2*).
- ❑ Set the time and date (*see Section 3*).
- ❑ Perform a control solution test (*see Section 4*).
- ❑ Insert your sensor (*see Section 5*).
- ❑ Attach your transmitter (*see Section 6*).
- ❑ Calibrate your receiver (*see Section 7*).
- ❑ Set the alarms in the receiver (*see Section 8*). **Note:** This can be done while waiting to perform the first calibration.

Result: *Your system is operational.*

Warnings, Cautions And Important Notes

Important Notes About System Performance

The following items describe situations that could lead to inaccurate or unreliable continuous glucose results.

Cautions:

- *Movement of the sensor support mount or excessive perspiration at the sensor insertion site due to activities like vigorous exercise or bumping against objects may lead to poor adhesion of the support mount to the skin and cause the sensor to dislodge. If the sensor dislodges due to the sensor support adhesive failing to adhere to the skin, you may get unreliable results or no results. The system may not provide a warning in such circumstances. Choose the proper sensor insertion site when inserting the sensor and prepare the site by following the instructions for site preparation.*
- *If your results from the Continuous Monitoring mode seem erroneous, check and make sure that the sensor has not dislodged. If you notice the sensor is dislodged from the skin, or if you see that the adhesive on your overbandage or the sensor support mount is coming loose, discard the old sensor and insert a new sensor.*
- *The FreeStyle Navigator system includes built-in self-checks to detect conditions that may cause the sensor to not function properly. On rare occasions the system may not be able to detect all such conditions (for example if the adhesive peels up from your skin), and you may get inaccurate results in the Continuous Monitoring mode. If you believe your results are not reliable, or are inconsistent with how you feel, perform a Blood Glucose mode test to measure your glucose. If the problem continues, discard the old sensor and insert a new sensor.*
- *You should never reset your user settings when you are wearing a sensor. This will reset parameters that may affect your system performance.*
- *If you accept an incorrect transmitter ID, your glucose readings will be incorrect.*
- *Do **NOT** use the sensor delivery unit if the sterile package is open or damaged.*

Important:

- *Once the code has been entered and you have hit the Set button, you will not be able to change the sensor code number. If you have entered the code incorrectly, you will have to replace the sensor and enter the right sensor code. If you choose the wrong sensor code, you may get erroneous results from the sensor. The code numbers MUST match to ensure accurate test results.*
- *Do **NOT** remove or replace the transmitter from the sensor support mount while wearing a sensor. If you notice that the transmitter is not properly attached, replace the sensor with a new sensor and then re-attach the transmitter.*

Important Things to Remember About System Calibration

***Caution:** Always calibrate the system using only a finger-stick blood sample. Do **NOT** use alternate site blood glucose measurements to calibrate the system. The receiver contains a built-in FreeStyle® Blood Glucose Meter for performing calibration tests.*

***Important:** Your blood glucose level must be between 60 and 300 mg/dL (3.3 and 16.6 mmol/L) to be able to perform calibration tests. If your blood glucose level is changing rapidly, you may not be able to calibrate the system. For example, during a meal or exercise, your glucose levels may vary rapidly. Try to time your sensor insertion so that your calibration times do not coincide with your regular meal or exercise activities.*

Important Things to Remember About System Calibration *(con't)*

Important: *In clinical trials, we observed that the sensor signal sometimes temporarily decreases from the true value. This typically happens at night during sleep, and recovers rapidly when the user moves or is awakened. However, in order to avoid being affected by this phenomenon the system should not be calibrated when the wearer is asleep.*

- You may not be able to calibrate the system if your glucose levels are changing rapidly. (e.g. during or after exercise, meals or insulin dosing). Under such conditions, the system may not ask you to calibrate; instead, it will delay its request until conditions are acceptable.
- You MUST successfully complete 4 calibration tests. You will calibrate at approximately 10, 12, 24 and 72 hours after sensor insertion. If you do not complete calibration tests successfully in the allotted time periods, your glucose readings will NOT be displayed and alarms will be inactive. The system may ask you to perform additional calibrations between 2nd and 3rd calibrations depending on the sensor signal. In such cases, you will be prompted with a message to do additional BG tests.
- The receiver will beep (or vibrate) to prompt you to do a calibration. The receiver will display a blood drop icon and the message "Do BG Test." The system will prompt you with alarm messages when your calibrations are unsuccessful.
- You will not have continuous monitoring until you have successfully completed the first calibration (at least for the first ten hours after sensor insertion).
- If you get a request for a calibration or expect additional calibration requests during a time when you do not want to be disturbed (e.g. sleep time), you can choose to wait to perform additional BG tests at a later point in time. If you choose to wait and the allotted time window for calibration has expired, please note that you will not get glucose results until you have performed a successful calibration. You can turn off the System Alarms (or set to vibrate) if you do not want to be disturbed by frequent requests for calibration. In order to silence the alarms that warn you when the allotted time window for a calibration has expired, you must turn off the data loss alarms and all the four glucose alarms (Low Glucose, High Glucose, Projected Low Glucose and Projected High Glucose).

Before You Get Started

Installation and operation of the FreeStyle Navigator® Continuous Glucose Monitoring System requires using a specialized introducer needle to insert the glucose sensor into the skin. Infection, inflammation, or bleeding at the glucose sensor insertion site are possible risks of inserting a sensor into your skin. The glucose sensor should be removed if redness, pain, tenderness, or swelling develops at the sensor insertion site.

Cautions:

- *Before adjusting treatment for diabetes management based on the continuous glucose results from your FreeStyle Navigator system, perform a Blood Glucose mode test to confirm the continuous result.*
- *A portion of the membrane polymer will remain in the skin each time the sensor is removed. Although no health effects were observed or reported in clinical studies, the long term effects of the sensor membrane fragments remaining in the skin have not been determined.*
- *Performance of the FreeStyle Navigator system has not been evaluated in pregnant women.*
- *Performance of the system under conditions of fluctuating hydration levels such as during renal dialysis has not been evaluated.*

Before You Get Started *(con't)*

Cautions:

- *Low or high glucose measurements can indicate a potentially serious medical condition.*
- *If you have hypoglycemia, or hypoglycemia unawareness, then test ONLY on your fingers.*
- *The high and low alarms are intended to assist you in managing your diabetes and should not be exclusively used to detect hypoglycemia or hyperglycemia. The alarms should always be used in conjunction with other indications of glycemic state such as your glucose level, trend, line graph etc.*
- *High and low glucose alarms are DIFFERENT from your glucose targets. Low and high glucose alarms alert you when you've crossed a certain low or high value. Glucose targets allow the reports and line graphs to show how your glucose levels have been performing compared to your set targets.*
- *The Low Glucose alarm will NOT indicate severe hypoglycemia because the alarm cannot be set below 60 mg/dL (3.3 mmol/L).*
- *The High Glucose alarm will NOT indicate severe hyperglycemia because the alarm cannot be set above 300 mg/dL (16.7 mmol/L).*
- *It is important to use the correct type of batteries in the receiver, otherwise the battery life may not be accurately monitored.*
- *Do NOT immerse the receiver in water or in any other liquid. Avoid getting water or any other liquid in the test strip port.*
- *Changes or modifications not expressly approved by Abbott Diabetes Care, Inc. could void the user's authority to operate the equipment.*
- *The system should not be used in an oxygen-rich environment or in one where anesthetic gas is present.*
- *The radio receiver and transmitter of your FreeStyle Navigator system operate on the frequency of 433.6 MHz. Primary users of this frequency band include amateur "HAM" radio transmitters. Because of the coexistence of the FreeStyle Navigator radio connection and HAM transmitters, there may be instances where the connection between your transmitter and receiver may be lost when in proximity to HAM radio equipment. The FreeStyle Navigator system is designed to sense and notify you about a lost connection. If your FreeStyle Navigator system loses the radio connection, increase the separation distance between yourself and the transmitter by moving away from the HAM radio. The FreeStyle Navigator radio connection should re-establish itself. You should note that HAM radio products can be fixed, mobile or portable handheld ("walkie talkie" type) units.*

Important: *Because you must insert a new sensor after each battery replacement, you should replace the batteries just before you insert a new sensor. For example, if you drop your receiver and the batteries fall out, you will have to insert a new sensor.*

Warnings:

Keep your system and its components away from young children because:

- There are small parts that may be dangerous if swallowed.
- The control solution caps are choking hazards.
- The test strip vial and sensor delivery unit packaging may contain a drying agent that could be harmful if inhaled or swallowed and may cause skin and eye irritation.

NEVER point a pre-cocked sensor inserter toward the eyes, face, or any other body part where sensor insertion is not desired.

Before You Get Started *(con't)*

- If your results from the continuous monitoring mode do not reflect how you feel, test your glucose using the Blood Glucose mode.
- If you observe a significant change in your continuous glucose readings that you think is erroneous, or if you feel the blood glucose measurement in the Blood Glucose mode is erroneous and you are close to an electromagnetic interference source, move away from the source of interference and check to see if the condition fades away.
- If you have a medical appointment that includes X-ray, MRI (Magnetic Resonance Imaging), CT (Computed Tomography) scan, or another type of exposure to radiation, keep your system and sensor away from the area. Before exposure to such radiation, discard any sensor you are wearing and insert a new sensor after the radiation session. The effect of these types of radiation on the performance of the system has not been evaluated.

Helpful health related information:

The following pertain to your health and should always be kept in mind:

- The system is intended to assist you in better managing your diabetes by allowing you to know your glucose levels throughout the day.
- Test results below 60 mg/dL (3.3 mmol/L) mean your glucose levels are low.
- Test results above 240 mg/dL (13.3 mmol/L) mean your glucose levels are high.
- Severe dehydration and excessive water loss may cause false low results. If you believe you are experiencing severe dehydration, consult your healthcare team immediately.
- If you get results below 60 mg/dL (3.3 mmol/L) or above 240 mg/dL (13.3 mmol/L) and do not have symptoms of hypoglycemia or hyperglycemia, test your glucose using the Blood Glucose mode.
- If you have symptoms of hypoglycemia or hyperglycemia, or continue to get results below 60 mg/dL (3.3 mmol/L) or above 240 mg/dL (13.3 mmol/L), consult your healthcare team.
- If you are experiencing symptoms that are not consistent with your glucose test results, consult your healthcare team. Physiologic differences between the interstitial fluid and capillary blood may result in differences in glucose measurements. Differences in glucose measurement between interstitial fluid and your finger may be observed during times of rapid change in blood glucose, e.g. after eating, dosing insulin, or exercising.
  - Interstitial fluid (ISF) is the fluid between cells in the body. Movement of nutrients, oxygen and glucose from the blood into the cells happen across the ISF. Therefore, if the glucose in the bloodstream rises (e.g. during meals), that rise is not seen in the ISF until later. Similarly, if glucose levels in the ISF drops (for example during exercise, the cells consume glucose rapidly) that drop is not seen in the bloodstream until later.
- When testing your glucose levels in the Blood Glucose mode, differences in the blood circulation in your finger or palm (at the base of your thumb) and other test sites (forearm, upper arm, hand, thigh, or calf) may result in different glucose readings. Differences in blood glucose readings between your finger or palm (at the base of your thumb) and other test sites (forearm, upper arm, hand, thigh, or calf) may be observed after eating, taking insulin, diabetes medication, or exercising.
- Test your finger if you are testing for hypoglycemia or if you have hypoglycemia unawareness (see next page for definition of hypoglycemia unawareness). Changes in glucose levels may be observed in finger blood samples sooner than in samples from alternative sites (forearm, upper arm, hand, thigh, or calf). If an alternate site must be used, vigorous rubbing of the alternate site before lancing can help minimize this difference.
- Do not use the FreeStyle Navigator system for diagnosing diabetes, testing newborns, or testing arterial or venous blood.

Section 18 – Appendix B

- Calibration
- Hematocrit Interstitial Fluid
- Receiver
- Transmitter

18 Appendix B: Specifications

System Specifications

Your FreeStyle Navigator system specifications are listed in the following table:

Operating Temperature	40° F to 104° F (4° C to 40° C).
Storage Temperature	14° F (-10° C) to 113° F (45° C). Store the sensor delivery unit, test strips between 37° F (3° C) and 86° F (30° C). Control solution should be stored between 50° F (10° C) and 86° F (30° C).
Operating Humidity (Receiver)	5% to 90% (non-condensing).
Operating and Storage Altitude	Sea level to 10,000 feet (3,048 meters).
Operating Pressure	14.7 psia (sea level) to 10.1 psia (10,000 feet).
Sensor Life	Up to 5 days.
Sensor Operating Skin Surface Temperature	77° F (25° C) to 104° F (40° C).
Glucose Result Range	20 to 500 mg/dL (1.1 to 27.8 mmol/L).
Glucose Assay Method (for CM mode)	Amperometric electrochemical sensor using WIRED ENZYME™ technology. Continuous subcutaneous measurement of glucose in interstitial fluid by a sensor inserted approximately 5mm under the skin.
Power Source	Transmitter: One silver oxide 357 HC battery (small coin cell battery), replaceable (battery life is ~ 30 days). Receiver: Two AAA alkaline batteries, replaceable (battery life is ~ 60 days). We recommend Energizer® MAX®, Energizer® e2® Titanium®, and Energizer® Industrial batteries. Other batteries may not provide expected battery life.
Transmitter Size	Height: 2.05 in. (5.2 cm). Width: 1.23 in. (3.1 cm). Depth: 0.43 in. (1.1 cm).
Transmitter Weight	0.48 oz. (13.61 grams) – including batteries.
Transmitter Battery Life	Up to 30 days.
Wearing Transmitter Under Water	Up to 1 meter under water for no more than 30 minutes.
Receiver Size	Height: 2.5 in. (6.3 cm). Width: 3.24 in. (8.2 cm). Depth: 0.88 in. (2.2 cm).

18 Appendix B: Specifications *(con't)*

Receiver Weight	3.5 oz. (99.2 grams) – including batteries.
Receiver Battery Life	Up to 60 days.
Automatic Shutoff	Built-in blood glucose meter: 2 minutes after last user action. Receiver: 12 seconds after last user action.
Receiver Memory	• 60 days of normal use including continuous glucose readings (stored every 10 minutes) and daily blood glucose readings. • Date/time will be remembered for 5 minutes after receiver battery removal.
Calibration	Plasma equivalent.
Calibration Time	• 1st calibration: Must be performed at approximately 10 hours after a new sensor has been inserted. The first calibration can be performed after the 10 hours. Continuous glucose readings will NOT be reported until the 1st calibration is performed successfully. • 2nd calibration: Must be performed between 2 and 4 hours after the 1st calibration or continuous glucose will not be reported. The 2nd calibration can be performed after 4 hours; continuous glucose reporting will resume after completing the 2nd calibration successfully. • 3rd calibration: Must be performed between 12 and 20 hours after the 2nd calibration or continuous glucose will not be reported. The 3rd calibration can be performed after 20 hours; continuous glucose reporting will resume after completing the 3rd calibration successfully. • 4th calibration: Must be performed between 48 and 56 hours after the third calibration or continuous glucose will not be reported. The fourth calibration can be performed after 56 hours; continuous glucose reporting will resume after completing the 4th calibration successfully.
Blood Glucose Test Time (for BG mode)	Average of 7 seconds.
Blood Glucose Assay Method (for BG mode)	Coulometric electrochemical sensor.
Blood Sample Type (for BG mode)	Whole blood, capillary.
Hematocrit (for BG mode)	15% to 65%.

18 Appendix B: Specifications *(con't)*

Performance Characteristics

Note: Please consult your healthcare team on how to use the information in this section.

Performance of the FreeStyle Navigator® Continuous Glucose Monitoring System was evaluated in a controlled clinical study. The study was conducted in 3 centers and included a total of 58 subjects with diabetes. Each subject wore two FreeStyle Navigator Sensors over a 5-day period. The subjects wore one sensor on the back of the upper arm and one on their abdomen. The FreeStyle Navigator system was calibrated with capillary finger-stick measurements using the built-in FreeStyle Blood Glucose Meter at approximately 10, 12, 24 and 72 hours after insertion of the sensor. All measurements were performed by a trained clinic study staff or the subject.

During the study, subjects came to the clinical center for frequent glucose samples measured once every 15 minutes on the YSI (Yellow Springs Instrument) STAT Plus™ Glucose Analyzer. YSI measurements were performed in duplicate on venous whole blood and the FreeStyle measurements were performed in duplicate on capillary blood from the finger. All YSI whole blood measurements were adjusted by applying a +12% correction factor (based on a normal hematocrit value of 45%).

Users and healthcare providers should consider that performance in this study might be idealized. Participants enrolled in the clinical study and certain conditions of the study tend to result in above average glucose control. This, in turn, may result in the appearance that the FreeStyle Navigator Continuous Glucose Monitoring System agrees with blood glucose levels better than it does under typical conditions. Monitors that measure glucose in interstitial fluid often show better agreement to blood glucose levels when glucose levels are not changing rapidly or when glucose levels are not extremely low or high. The following are some examples of why performance of the FreeStyle Navigator Continuous Glucose Monitoring System may be idealized.

- Subjects saw, on average, 15 fingerstick results per day in the clinic and 8 fingerstick results per day at home. This enables subjects to control their glucose levels better.
- While subjects participated in the clinic portion of the study, they were more limited in their activities than someone at home. They were also provided with all their meals. Subjects who are more active, or with poor eating habits, may create more challenging conditions for the FreeStyle Navigator Continuous Glucose Monitoring System.
- The built-in FreeStyle glucose meters used in the study were well maintained. Because the built-in FreeStyle meter is used to calibrate the FreeStyle Navigator Continuous Glucose Monitoring System, performance may be poorer if the system is not well maintained. It is important to carry out quality-control checks on the system and code the system according to the manufacturer's instructions to optimize performance of the FreeStyle Navigator Continuous Glucose Monitoring System.

Accuracy

Table 1 below shows the distribution of all the data from the In-Clinic study on the Clarke Error Grid. Accuracy was assessed by comparing the differences between the FreeStyle Navigator system and the YSI laboratory reference. The Clarke Error Grid Analysis evaluates the clinical relevance of the differences by dividing a correlation plot (Figure 1) into five zones as described in Table 1. The YSI results and the corresponding glucose results from the FreeStyle Navigator system together (called a 'data pair' or 'matched data points') determine what zone of the error grid the results fall into. Table 1 also shows that glucose data measured by FreeStyle Navigator system on the arm and on the abdomen have similar distribution on the error grid. This demonstrates that there is no difference in the performance of the system when worn on the abdomen or on the back of the upper arm.

Table 1. Clarke Error Grid Analysis. Continuous glucose results from FreeStyle Navigator System (mg/dL) vs. the YSI (mg/dL)

Zone in the Clarke Error Grid	N (pairs of data)	Percentage in the different zones (%)	Sensor Insertion Site	
			Abdomen %	Arm %
A	16627	81.7	81.5	81.8
B	3398	16.7	16.8	16.6
C	19	0.1	0.1	0.1
D	316	1.6	1.6	1.5
E	2	0.0	0.0	0.0
Total	20362	There is no difference between the performance of the system on the arm and the performance of the system on the abdomen.		

Error Grid Explanation
A - Clinically accurate; would lead to correct and safe treatment
B - Benign; would lead to benign decisions or no treatment decisions
C - Overcorrection; would lead to overcorrection of normal glucose levels
D - Failure to detect; would lead to failure to detect and treat high or low glucose levels
E - Erroneous readings; would lead to erroneous treatment decisions

18 Appendix B: Specifications *(con't)*

Table 2 is a summary of the statistics that describe how well data from the FreeStyle Navigator system correlates to the results from the reference method. Glucose results from the FreeStyle Navigator system and the corresponding results from the YSI (a total 20362 pairs of data points) in the In-Clinic study were used to determine the correlation.

Figure 1.

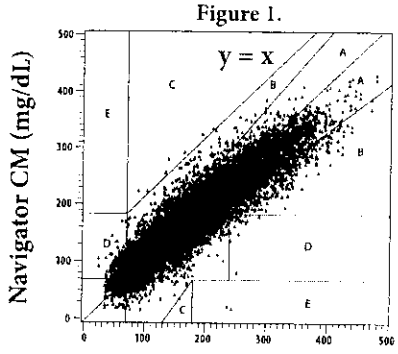


Table 2. Regression Analysis. FreeStyle Navigator System (mg/dL) vs the YSI (mg/dL)

Slope	0.92
Intercept	14.3 mg/dL
Correlation Coefficient (r)	0.93
N	20362
Range	25 – 533 mg/dL
Overall mean bias	+0.8 mg/dL

Table 3a displays the distribution of all the data from the In-Clinic study on the Clarke Error Grid. It breaks the data set into smaller groups based on the glucose value reported by the YSI. For each of these smaller groups, the table shows what percentage of data fall into different zones of the grid.

Table 3a. Accuracy performance at different glucose levels using the Clarke Error Grid Analysis

Reference Glucose Level (mg/dL)	Number of Paired Readings	A and B (%)	A (%)	B (%)	C (%)	D (%)	E (%)
20-40	22	54.5	54.5	N/A*	N/A*	45.5	0.0
41-80	1295	77.7	55.2	22.5	0.0	22.3	0.0
81-120	3820	99.9	69.5	30.4	0.1	N/A*	N/A*
121-240	11430	99.9	85.4	14.4	0.1	N/A*	0.0
241+	3795	99.5	91.7	7.8	0.0	0.4	0.1
Overall	**20362**	98.3	**81.7**	**16.7**	**0.1**	**1.6**	**0.0**

*N/A means that the Clarke Error Grid does not consider the possibility of these zones in that concentration range.

Table 3b displays the same data as in table 3a on the Continuous Glucose-Error Grid. This is a modified error grid that is designed to evaluate the clinical accuracy of continuous glucose monitoring systems based on both glucose data points in time and the rate of change of glucose.

Table 3b. Accuracy performance at different glucose levels using the Continuous Glucose-Error Grid Analysis

Zone	YSI ≤ 70 mg/dL		70 mg/dL < YSI ≤180 mg/dL		YSI > 180 mg/dL		All	
	N	%	N	%	N	%	N	%
Accurate Readings	369	59.5	10407	98.9	8364	98.6	19140	97.5
Benign Errors	5	0.8	99	0.9	74	0.9	178	0.9
Erroneous Readings	246	39.7	22	0.2	41	0.5	309	1.6
ALL	620	100.0	10528	100.0	8479	100.0	19627	100.0

18 Appendix B: Specifications *(con't)*

Performance Relative to the Reference (YSI)

Error grid analysis (like the Clarke Error Grid Analysis and Continuous Glucose-Error Grid Analysis) is one way to evaluate the accuracy of the FreeStyle Navigator system. The accuracy can also be assessed by analyzing the difference in the glucose results from the FreeStyle Navigator system when compared to the results from the YSI. Table 4a shows an analysis of the measure of closeness of the FreeStyle Navigator system to the YSI. It breaks the data into smaller groups based on the glucose value reported by the YSI. The table reports the mean absolute difference for the data pairs in each of the smaller groups. Table 4b shows the same data at different levels of glucose and further groups them by the amount of difference from the YSI. Table 5 breaks out the overall performance relative to the YSI for the two sites of sensor insertion.

The overall median absolute relative difference for all the data pairs is **9.3%**.

Table 4a. Performance relative to YSI at different glucose levels

Glucose (mg/dL)	Performance
20-40	Mean Absolute Difference = 32.3 mg/dL
41-80	Mean Absolute Difference = 18.1 mg/dL
81-120	Mean Absolute Difference = 16.3 mg/dL
121-240	Mean Absolute Relative Difference = 11.0%
>240	Mean Absolute Relative Difference = 9.5%

Table 4b. Performance relative to YSI at different levels of glucose – grouped by amount of difference from the YSI

Glucose Range (mg/dL)	Number of Paired Readings	Percent Within 20% of the YSI	Percent Within 30% of the YSI	Percent Within 40% of the YSI
20-40*	22	31.8	54.5	72.7
41-80*	1295	65.9	82.0	90.7
81-120	3820	69.5	85.2	92.7
121-240	11430	85.4	95.1	98.3
>241	3795	91.7	98.8	99.9
Overall	20362	82.3	93.1	97.0

*The absolute difference from the YSI reading is measured in mg/dL if the YSI reading is 20-80 mg/dL.

Table 5. Performance relative to YSI at different insertion sites

Overall MeanAbsolute RelativeDifference	MARD by Insertion Site	
	Abdomen	Arm
12.8% (Std. Dev. = 13.6%)	13.1%	12.6%

18 Appendix B: Specifications *(con't)*

Performance Over the Duration of Wear

This section presents the performance data in a variety of ways to demonstrate the performance of the system over time during the entire sensor wear period. The sensor is worn on the body for up to 5 days, during which time the system has to be calibrated 4 times. Typically, the system has to be calibrated at 10, 12, 24 and 72 hours after sensor insertion. Data presented in this section demonstrates how the sensor performs as a function of time.

Sensor Stability

Tables 6a-6b show there is little difference in accuracy over the five days of sensor wear according to the Clarke Error Grid Analysis (Table 6a) and the Continuous Glucose-Error Grid Analysis (Table 6b).

Table 6a. Clarke Error Grid Analysis by day of wear

Zone	Day 1	Day 2	Day 3	Day 4	Day 5
	%	%	%	%	%
A	82.5	82.4	79.4	84.0	80.9
B	16.4	16.6	18.3	14.2	16.9
C	0.2	0.1	0.0	0.0	0.0
D	0.9	0.9	2.2	1.8	2.1
E	0.0	0.1	0.0	0.0	0.0
Overall Mean Absolute Relative Difference (%) MARD0	12.6	12.3	14.1	11.9	13.0

Table 6b. Continuous Error Grid Analysis by day of wear

Zone	Day 1	Day 2	Day 3	Day 4	Day 5
	%	%	%	%	%
Accurate Readings	97.9	97.8	97.1	97.4	97.3
Benign Errors	1.0	1.2	0.7	0.8	0.8
Erroneous Readings	1.1	1.0	2.2	1.8	1.9

Table 6c groups the difference between glucose results from the FreeStyle Navigator system and the YSI into different blocks (within 20%, within 30% and within 40% from the YSI). It shows there is little change in the difference from YSI over time, thus demonstrating sensor stability.

Table 6c. Difference from the YSI at different times after sensor insertion

Time After Insertion (hours)	Percent Readings Within 20% of the YSI*	Percent Readings Within 30% of the YSI*	Percent Readings Within 40% of the YSI*
10-12	86	92	96
12-24	82	93	97
24-72	81	92	97
72-122	82	93	97

*The absolute difference from the YSI reading is measured in mg/dL if the YSI reading is at or below 75 mg/dL.

18 Appendix B: Specifications *(con't)*

Stability of Sensor Calibration

FreeStyle Navigator system typically requires a calibration at 10, 12, 24 and 72 hours after insertion of the sensor. This section presents information about the performance of the system by the 4 calibration periods. The table (Table 6d) breaks each calibration period into smaller slots and summarizes the difference from YSI in each slot. The data below demonstrates that there is little change in the system performance within each period.

Table 6d. Distribution of the difference from the YSI in the different calibration windows

Calibration Period		Percent Readings Within 20%* of the YSI	Percent Readings Within 30%* of the YSI	Percent Readings Within 40%* of the YSI
Cal 1 (typically occurs 10 hrs after sensor insertion)	First Calibration Period	80	88	94
Cal 2 (typically occurs 12 hours after sensor insertion)	First Third of Second Calibration Period	83	94	98
	Second Third of Second Calibration Period	83	94	98
	Final Third of Second Calibration Period	84	95	98
Cal 3 (typically occurs 24 hours after sensor insertion)	First Third of Third Calibration Period	84	94	98
	Second Third of Third Calibration Period	80	92	97
	Final Third of Third Calibration Period	80	91	95
Cal 4 (typically occurs 72 hours after sensor insertion)	First Quarter of Final Calibration Period	86	93	96
	Second Quarter of Final Calibration Period	84	92	96
	Third Quarter of Final Calibration Period	80	93	98
	Final Quarter of Final Calibration Period	82	93	97

* The absolute difference from the YSI reading is measured in mg/dL if the YSI reading is at or below 75 mg/dL.

Sample Glucose Traces

The following figures show examples of glucose traces from the In-Clinic study. These traces are representative examples of excellent, average and poor performance of the system. These traces show an overlay of the continuous glucose readings from the FreeStyle Navigator system and the blood glucose measurements made using the laboratory YSI reference. The blood glucose measurements that were used to calibrate the system are marked with 'x' in the traces. Glucose results from the FreeStyle Navigator system are shown using circles and the glucose results from the laboratory reference (YSI) are shown using triangles. Time (hours since sensor insertion) is on the horizontal axis, and glucose value in mg/dL is on the vertical axis.

18 Appendix B: Specifications *(con't)*

Figure 2. Sample of a Representative 'Excellent' Glucose Trace

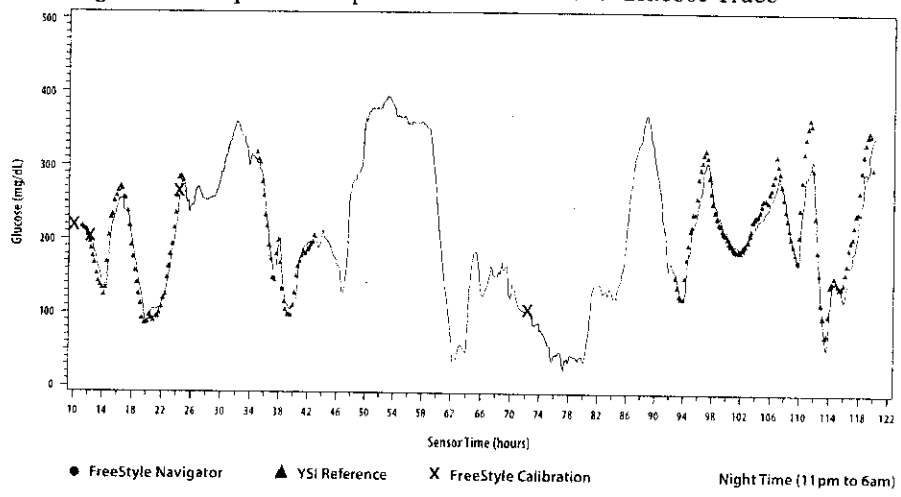


Figure 3. Sample of a Representative 'Average' Glucose Trace

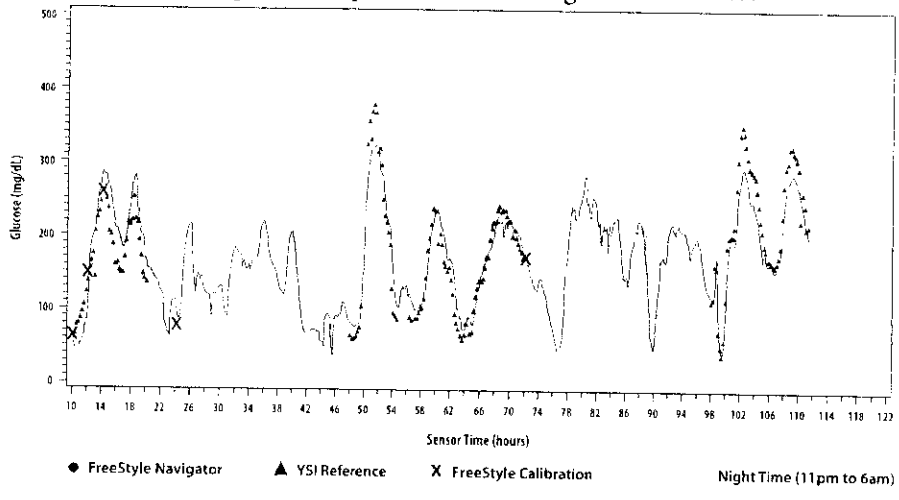
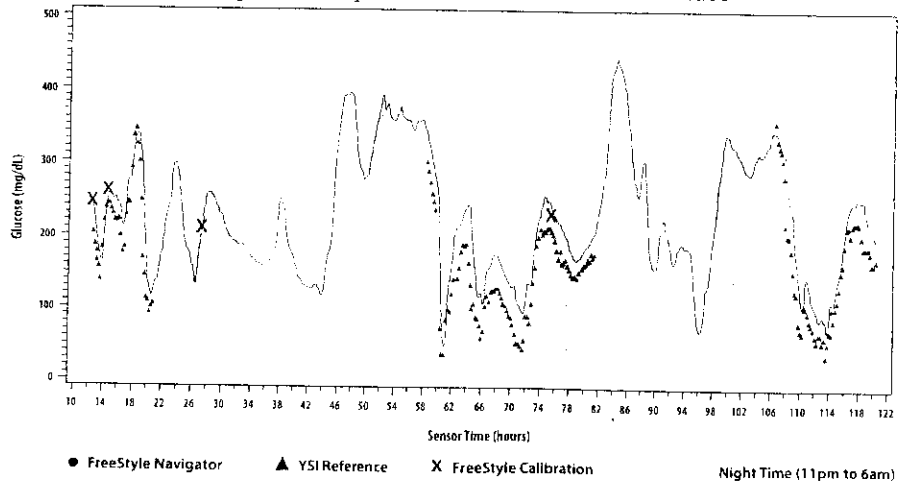


Figure 4. Sample of a Representative 'Poor' Glucose Trace



18 Appendix B: Specifications *(con't)*

Determination of Alarm Performance

The threshold alarm is characterized belowhere. The projected alarm performance has not been established.

The performance of low and high glucose alarms was assessed in an in-clinic study using 58 subjects with type 1 diabetes wearing one FreeStyle Navigator sensor on the arm and one sensor on the abdomen. FreeStyle Navigator continuous data were masked from the subjects and investigators and the alarms were not turned on. During 50 hours the subjects' venous glucose was tested with a YSI 2300 Stat Plus glucose analyzer at 15 minute intervals. Arm and abdomen data were pooled in the alarm analysis. Alarm performance was evaluated in a retrospective analysis of the study data. As alarm performance was developed retrospectively, your results may vary from those reported below.

Definitions:

Hypoglycemic event – two or more successive YSI measurements below the alarm threshold or one YSI measurement 6 mg/dL below the alarm threshold.

Hyperglycemic event - two or more successive YSI measurements above the alarm threshold or one YSI measurement 6% above the alarm threshold.

True Threshold Alarm – a threshold alarm that occurred ± 30 minutes from the start of a hypoglycemic or hyperglycemic event

True Alarm Rate – the percentage of time the glucose level was beyond the threshold and an alarm was activated

$$\frac{\text{Events Detected by True Threshold Alarms}}{\text{Total Events}} \times 100$$

Missed Alarm Rate - the percentage of time the glucose level was beyond the threshold and an alarm was not activated

$$\frac{\text{Events Not Detected By True Threshold Alarms}}{\text{Total Events}} \times 100$$

False Threshold Alarm – a threshold alarm that occurred when a YSI measurement within ± 30 minutes was not beyond the threshold setting

False Alarm Rate – the percentage of time an alarm occurred when glucose level was not beyond the threshold setting

$$\frac{\text{False Threshold Alarms}}{\text{Total Threshold Alarms}} \times 100$$

Detection of Low Glucose

See Table 7 below for detection of low glucose. As an example, when the threshold alarm was set at 70 mg/dL (during the day), 56 % of the low glucose events were detected by FreeStyle Navigator.

Table 7 Low Glucose Detection

	DAY			NIGHT		
Low Alarm Setting (mg/dL)	**Day True Alarms***	**Day Missed Alarms****	**Day False Alarms*****	**Night True Alarms***	**Night Missed Alarms****	**Night False Alarms*****
	% (n/N†)	**% (n/N)**	**% (n/N)**	**% (n/N)**	**% (n/N)**	**% (n/N)**
65	46 (56/121)	54 (65/121)	19 (18/95)	80 (12/15)	20 (3/15)	41 (11/27)
70	56 (98/176)	44 (78/176)	16 (21/132)	79 (19/24)	21 (5/24)	40 (14/35)
75	59 (130/219)	41 (89/219)	9 (15/161)	72 (23/32)	28 (9/32)	37 (14/38)
85	61 (189/308)	39 (119/308)	7 (17/228)	65 (22/34)	35 (12/34)	33 (14/43)

* True Alarms are the percentage of time the glucose level was below the threshold and an alarm was activated
**Missed Alarms are the percentage of time the glucose level was below the threshold and an alarm was not activated.
***False Alarms are the percentage of time an alarm occurred but the glucose level was not below the threshold setting.
†n/N is the (n)umber of observations divided by the total (N)umber

18 Appendix B: Specifications *(con't)*

Detection of High Glucose

See Table 8 for detection of high glucose. As an example, when the threshold alarm was set at 240 mg/dL (during the day), 78 % of the high glucose events were detected by FreeStyle Navigator.

Table 8 High Glucose Detection

	DAY			NIGHT		
High Alarm Setting (mg/dl.	Day True Alarms*	Day Missed Alarms**	Day False Alarms*	Night True Alarms**	Night Missed Alarms***	Night False Alarms***
	% (n/N†)	% (n/N)	% (n/N)	% (n/N)	% (n/N)	% (n/N)
180	89 (561/630)	11 (69/630)	11 (68/628)	69 (29/42)	31 (13/42)	7 (3/44)
240	78 (295/376)	22 (81/376)	12 (47/393)	41 (12/29)	59 (17/29)	25 (7/28)
270	70 (193/274)	30 (81/274)	12 (32/265)	21 (3/14)	79 (11/14)	36 (5/14)
300	61 (117/192)	39 (75/192)	12 (20/161)	12 (1/8)	88 (7/8)	33 (1/3)

* True Alarms are the percentage of time the glucose level was above the threshold and an alarm was activated
**Missed Alarms are the percentage of time the glucose level was above the threshold and an alarm was not activated.
***False Alarms are the percentage of time an alarm occurred but the glucose level was not above the threshold setting
†n/N is the (n)umber of observations divided by the total (N)umber

18 Appendix B: Specifications *(con't)*

Measuring Glucose in Interstitial Fluid

FreeStyle Navigator system measures glucose in the interstitial fluid (ISF) by means of a sensor that is inserted about 5 mm under the skin. Interstitial fluid is the fluid between the body's cells. Physiologic differences between the interstitial fluid and capillary blood may result in differences in glucose measurements. Differences in glucose measurement between interstitial fluid and your finger may be observed during times of rapid change in blood glucose, e.g. after eating, dosing insulin, or exercising. Movement of nutrients, oxygen and glucose from the blood into the cells happen across the ISF.

Therefore, if the glucose in the bloodstream rises (e.g. during meals), that rise is not seen in the ISF until later. Similarly, if glucose levels in the ISF drop (for example during exercise, the cells consume glucose rapidly) that drop is not seen in the bloodstream until later.

On average, glucose levels in the ISF lag the glucose levels in capillary blood by 14 minutes. This is a physiological phenomenon that can vary from one person to another.

Precision

Data from two sensors inserted at different insertion sites was used to calculate the between sensor reproducibility. Based on 312953 pairs of data sets, the average between sensor reproducibility was 10%.

Sensor Insertion, Calibration and Sensor Wear

Home Use Study: Sensor insertion, calibration and sensor wear were evaluated in a Home Use Study where 137 participants used the product on their own in a home environment. The participants wore 8 sensors during the study period of 40 days. They wore the sensors either on the arm or abdomen. During the first 20 days of the study, continuous glucose results were not visible to the participants. During the following 20 days, participants had access to the glucose measurements. In addition to required calibration tests, the participants performed 4 finger stick measurements a day using the built-in FreeStyle meter. The following information is based on the findings from this study.

When used as directed, 96.8% of the total sensor insertions were successful. 92.6% of the sensors were calibrated successfully and began producing glucose results within 12 hours after sensor insertion. The median time for a successful first calibration was 10.1 hours. The median duration of wear of calibrated sensors was 120 hours. 83% of sensor wears lasted at least 108.3 hours. The median wear time for sensors inserted on the arm was 0.4 hours longer than for sensors inserted on the abdomen.

Skin Interaction

Based on the examination of 124 study participants at a 21-day follow up, the following incidence of skin issues were observed in 304 site exams.
Moderate to severe itching – 1.6% of the time
Moderate bruising – 0.3% of the time
Moderate erythema – 1.0% of the time
Moderate pain – 0.3% of the time
Rate of mild incidences for any individual category of skin issues above including edema, rash, induration, bleeding and others was less than 5%.

What is Hypoglycemia Unawareness?

Hypoglycemia unawareness is a condition where you are having hypoglycemia but you do not have any of the usual warning symptoms (such as rapid heartbeat, sweating, shakiness, anxiety, or a tingling sensation in your fingers or toes). Those warning symptoms are either absent or greatly reduced. Instead, the first sign may be confusion or impaired thinking, which makes it even more difficult to know if you are experiencing low blood glucose. You could find yourself in the midst of a severe hypoglycemic episode without any warning at all.

Symptoms of Hypoglycemia Unawareness:

Because you would have missed the early warning signs of hypoglycemia, the only signs or symptoms you may have would be due to the effects of low blood glucose on the brain:

- Irritability
- Tiredness
- Confusion
- Forgetfulness
- Pale skin
- Slurred speech
- Loss of consciousness

This condition is potentially dangerous because hypoglycemia confusion can occur without warning.

If you were driving a car or operating heavy machinery, confusion or delayed reaction could cause an accident.

Hypoglycemia unawareness can develop for several reasons:

a. Having frequent hypoglycemic episodes.

b. Having long standing diabetes and autonomic neuropathy (a form of diabetic neuropathy in which your body does not release its usual hormones to warn you of low blood glucose and to tell your liver to release glucose as a protective mechanism).

If you think you have hypoglycemia unawareness, talk to your healthcare team.

Section 18 – Appendix B

- Calibration
- Hematocrit Interstitial Fluid
- Receiver
- Transmitter

18 Appendix B: Specifications

System Specifications

Your FreeStyle Navigator system specifications are listed in the following table:

Operating Temperature	40° F to 104° F (4° C to 40° C).
Storage Temperature	14° F (-10° C) to 113° F (45° C). Store the sensor delivery unit, test strips between 37° F (3° C) and 86° F (30° C). Control solution should be stored between 50° F (10° C) and 86° F (30° C).
Operating Humidity (Receiver)	5% to 90% (non-condensing).
Operating and Storage Altitude	Sea level to 10,000 feet (3,048 meters).
Operating Pressure	14.7 psia (sea level) to 10.1 psia (10,000 feet).
Sensor Life	Up to 5 days.
Sensor Operating Skin Surface Temperature	77° F (25° C) to 104° F (40° C).
Glucose Result Range	20 to 500 mg/dL (1.1 to 27.8 mmol/L).
Glucose Assay Method (for CM mode)	Amperometric electrochemical sensor using WIRED ENZYME™ technology. Continuous subcutaneous measurement of glucose in interstitial fluid by a sensor inserted approximately 5mm under the skin.
Power Source	Transmitter: One silver oxide 357 HC battery (small coin cell battery), replaceable (battery life is ~ 30 days). Receiver: Two AAA alkaline batteries, replaceable (battery life is ~ 60 days). We recommend Energizer® MAX®, Energizer® e2® Titanium®, and Energizer® Industrial batteries. Other batteries may not provide expected battery life.
Transmitter Size	Height: 2.05 in. (5.2 cm). Width: 1.23 in. (3.1 cm). Depth: 0.43 in. (1.1 cm).
Transmitter Weight	0.48 oz. (13.61 grams) - including batteries.
Transmitter Battery Life	Up to 30 days.
Wearing Transmitter Under Water	Up to 1 meter under water for no more than 30 minutes.
Receiver Size	Height: 2.5 in. (6.3 cm). Width: 3.24 in. (8.2 cm). Depth: 0.88 in. (2.2 cm).

18 Appendix B: Specifications *(con't)*

Receiver Weight	3.5 oz. (99.2 grams) – including batteries.
Receiver Battery Life	Up to 60 days.
Automatic Shutoff	Built-in blood glucose meter: 2 minutes after last user action. Receiver: 12 seconds after last user action.
Receiver Memory	• 60 days of normal use including continuous glucose readings (stored every 10 minutes) and daily blood glucose readings. • Date/time will be remembered for 5 minutes after receiver battery removal.
Calibration	Plasma equivalent.
Calibration Time	• 1st calibration: Must be performed at approximately 10 hours after a new sensor has been inserted. The first calibration can be performed after the 10 hours. Continuous glucose readings will NOT be reported until the 1st calibration is performed successfully. • 2nd calibration: Must be performed between 2 and 4 hours after the 1st calibration or continuous glucose will not be reported. The 2nd calibration can be performed after 4 hours; continuous glucose reporting will resume after completing the 2nd calibration successfully. • 3rd calibration: Must be performed between 12 and 20 hours after the 2nd calibration or continuous glucose will not be reported. The 3rd calibration can be performed after 20 hours; continuous glucose reporting will resume after completing the 3rd calibration successfully. • 4th calibration: Must be performed between 48 and 56 hours after the third calibration or continuous glucose will not be reported. The fourth calibration can be performed after 56 hours; continuous glucose reporting will resume after completing the 4th calibration successfully.
Blood Glucose Test Time (for BG mode)	Average of 7 seconds.
Blood Glucose Assay Method (for BG mode)	Coulometric electrochemical sensor.
Blood Sample Type (for BG mode)	Whole blood, capillary.
Hematocrit (for BG mode)	15% to 65%.

18 Appendix B: Specifications *(con't)*

Performance Characteristics

Note: Please consult your healthcare team on how to use the information in this section.

Performance of the FreeStyle Navigator® Continuous Glucose Monitoring System was evaluated in a controlled clinical study. The study was conducted in 3 centers and included a total of 58 subjects with diabetes. Each subject wore two FreeStyle Navigator Sensors over a 5-day period. The subjects wore one sensor on the back of the upper arm and one on their abdomen. The FreeStyle Navigator system was calibrated with capillary finger-stick measurements using the built-in FreeStyle Blood Glucose Meter at approximately 10, 12, 24 and 72 hours after insertion of the sensor. All measurements were performed by a trained clinic study staff or the subject.

During the study, subjects came to the clinical center for frequent glucose samples measured once every 15 minutes on the YSI (Yellow Springs Instrument) STAT Plus™ Glucose Analyzer. YSI measurements were performed in duplicate on venous whole blood and the FreeStyle measurements were performed in duplicate on capillary blood from the finger. All YSI whole blood measurements were adjusted by applying a +12% correction factor (based on a normal hematocrit value of 45%).

Users and healthcare providers should consider that performance in this study might be idealized. Participants enrolled in the clinical study and certain conditions of the study tend to result in above average glucose control. This, in turn, may result in the appearance that the FreeStyle Navigator Continuous Glucose Monitoring System agrees with blood glucose levels better than it does under typical conditions. Monitors that measure glucose in interstitial fluid often show better agreement to blood glucose levels when glucose levels are not changing rapidly or when glucose levels are not extremely low or high. The following are some examples of why performance of the FreeStyle Navigator Continuous Glucose Monitoring System may be idealized.

- Subjects saw, on average, 15 fingerstick results per day in the clinic and 8 fingerstick results per day at home. This enables subjects to control their glucose levels better.
- While subjects participated in the clinic portion of the study, they were more limited in their activities than someone at home. They were also provided with all their meals. Subjects who are more active, or with poor eating habits, may create more challenging conditions for the FreeStyle Navigator Continuous Glucose Monitoring System.
- The built-in FreeStyle glucose meters used in the study were well maintained. Because the built-in FreeStyle meter is used to calibrate the FreeStyle Navigator Continuous Glucose Monitoring System, performance may be poorer if the system is not well maintained. It is important to carry out quality-control checks on the system and code the system according to the manufacturer's instructions to optimize performance of the FreeStyle Navigator Continuous Glucose Monitoring System.

Accuracy

Table 1 below shows the distribution of all the data from the In-Clinic study on the Clarke Error Grid. Accuracy was assessed by comparing the differences between the FreeStyle Navigator system and the YSI laboratory reference. The Clarke Error Grid Analysis evaluates the clinical relevance of the differences by dividing a correlation plot (Figure 1) into five zones as described in Table 1. The YSI results and the corresponding glucose results from the FreeStyle Navigator system together (called a 'data pair' or 'matched data points') determine what zone of the error grid the results fall into. Table 1 also shows that glucose data measured by FreeStyle Navigator system on the arm and on the abdomen have similar distribution on the error grid. This demonstrates that there is no difference in the performance of the system when worn on the abdomen or on the back of the upper arm.

Table 1. Clarke Error Grid Analysis. Continuous glucose results from FreeStyle Navigator System (mg/dL) vs. the YSI (mg/dL)

Zone in the Clarke Error Grid	N (pairs of data)	Percentage in the different zones (%)	Sensor Insertion Site	
			Abdomen %	Arm %
A	16627	81.7	81.5	81.8
B	3398	16.7	16.8	16.6
C	19	0.1	0.1	0.1
D	316	1.6	1.6	1.5
E	2	0.0	0.0	0.0
Total	20362	There is no difference between the performance of the system on the arm and the performance of the system on the abdomen.		

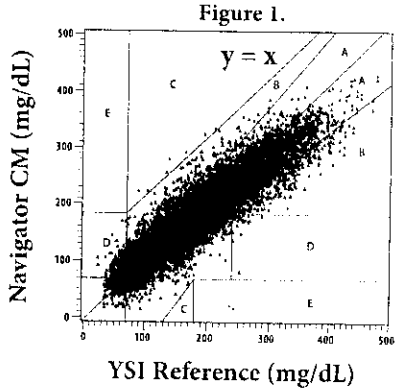
Error Grid Explanation
A - Clinically accurate; would lead to correct and safe treatment
B - Benign; would lead to benign decisions or no treatment decisions
C - Overcorrection; would lead to overcorrection of normal glucose levels
D - Failure to detect; would lead to failure to detect and treat high or low glucose levels
E - Erroneous readings; would lead to erroneous treatment decisions

OVER

18 Appendix B: Specifications *(con't)*

Table 2 is a summary of the statistics that describe how well data from the FreeStyle Navigator system correlates to the results from the reference method. Glucose results from the FreeStyle Navigator system and the corresponding results from the YSI (a total 20362 pairs of data points) in the In-Clinic study were used to determine the correlation.

Figure 1.



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Slope	0.92
Intercept	14.3 mg/dL
Correlation Coefficient (r)	0.93
N	20362
Range	25 - 533 mg/dL
Overall mean bias	+0.8 mg/dL

Table 3a displays the distribution of all the data from the In-Clinic study on the Clarke Error Grid. It breaks the data set into smaller groups based on the glucose value reported by the YSI. For each of these smaller groups, the table shows what percentage of data fall into different zones of the grid.

Table 3a. Accuracy performance at different glucose levels using the Clarke Error Grid Analysis

Reference Glucose Level (mg/dL)	Number of Paired Readings	A and B (%)	A (%)	B (%)	C (%)	D (%)	E (%)
20-40	22	54.5	54.5	N/A*	N/A*	45.5	0.0
41-80	1295	77.7	55.2	22.5	0.0	22.3	0.0
81-120	3820	99.9	69.5	30.4	0.1	N/A*	N/A*
121-240	11430	99.9	85.4	14.4	0.1	N/A*	0.0
241+	3795	99.5	91.7	7.8	0.0	0.4	0.1
Overall	**20362**	98.3	**81.7**	**16.7**	**0.1**	**1.6**	**0.0**

*N/A means that the Clarke Error Grid does not consider the possibility of these zones in that concentration range.

Table 3b displays the same data as in table 3a on the Continuous Glucose-Error Grid. This is a modified error grid that is designed to evaluate the clinical accuracy of continuous glucose monitoring systems based on both glucose data points in time and the rate of change of glucose.

Table 3b. Accuracy performance at different glucose levels using the Continuous Glucose-Error Grid Analysis

Zone	YSI ≤ 70 mg/dL		70 mg/dL < YSI ≤180 mg/dL		YSI > 180 mg/dL		All	
	N	%	N	%	N	%	N	%
Accurate Readings	369	59.5	10407	98.9	8364	98.6	19140	97.5
Benign Errors	5	0.8	99	0.9	74	0.9	178	0.9
Erroneous Readings	246	39.7	22	0.2	41	0.5	309	1.6
ALL	620	100.0	10528	100.0	8479	100.0	19627	100.0

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Performance Relative to the Reference (YSI)

Error grid analysis (like the Clarke Error Grid Analysis and Continuous Glucose-Error Grid Analysis) is one way to evaluate the accuracy of the FreeStyle Navigator system. The accuracy can also be assessed by analyzing the difference in the glucose results from the FreeStyle Navigator system when compared to the results from the YSI. Table 4a shows an analysis of the measure of closeness of the FreeStyle Navigator system to the YSI. It breaks the data into smaller groups based on the glucose value reported by the YSI. The table reports the mean absolute difference for the data pairs in each of the smaller groups. Table 4b shows the same data at different levels of glucose and further groups them by the amount of difference from the YSI. Table 5 breaks out the overall performance relative to the YSI for the two sites of sensor insertion.

The overall median absolute relative difference for all the data pairs is **9.3%**.

Table 4a. Performance relative to YSI at different glucose levels

Glucose (mg/dL)	Performance
20-40	Mean Absolute Difference = 32.3 mg/dL
41-80	Mean Absolute Difference = 18.1 mg/dL
81-120	Mean Absolute Difference = 16.3 mg/dL
121-240	Mean Absolute Relative Difference = 11.0%
>240	Mean Absolute Relative Difference = 9.5%

Table 4b. Performance relative to YSI at different levels of glucose – grouped by amount of difference from the YSI

Glucose Range (mg/dL)	Number of Paired Readings	Percent Within 20% of the YSI	Percent Within 30% of the YSI	Percent Within 40% of the YSI
20-40*	22	31.8	54.5	72.7
41-80*	1295	65.9	82.0	90.7
81-120	3820	69.5	85.2	92.7
121-240	11430	85.4	95.1	98.3
>241	3795	91.7	98.8	99.9
Overall	20362	82.3	93.1	97.0

*The absolute difference from the YSI reading is measured in mg/dL if the YSI reading is 20-80 mg/dL.

Table 5. Performance relative to YSI at different insertion sites

Overall MeanAbsolute RelativeDifference	MARD by Insertion Site	
	Abdomen	Arm
12.8% (Std. Dev. = 13.6%)	13.1%	12.6%

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Performance Over the Duration of Wear

This section presents the performance data in a variety of ways to demonstrate the performance of the system over time during the entire sensor wear period. The sensor is worn on the body for up to 5 days, during which time the system has to be calibrated 4 times. Typically, the system has to be calibrated at 10, 12, 24 and 72 hours after sensor insertion. Data presented in this section demonstrates how the sensor performs as a function of time.

Sensor Stability

Tables 6a-6b show there is little difference in accuracy over the five days of sensor wear according to the Clarke Error Grid Analysis (Table 6a) and the Continuous Glucose-Error Grid Analysis (Table 6b).

Table 6a. Clarke Error Grid Analysis by day of wear

Zone	Day 1	Day 2	Day 3	Day 4	Day 5
	%	%	%	%	%
A	82.5	82.4	79.4	84.0	80.9
B	16.4	16.6	18.3	14.2	16.9
C	0.2	0.1	0.0	0.0	0.0
D	0.9	0.9	2.2	1.8	2.1
E	0.0	0.1	0.0	0.0	0.0
Overall Mean Absolute Relative Difference (%) MARD0	12.6	12.3	14.1	11.9	13.0

Table 6b. Continuous Error Grid Analysis by day of wear

Zone	Day 1	Day 2	Day 3	Day 4	Day 5
	%	%	%	%	%
Accurate Readings	97.9	97.8	97.1	97.4	97.3
Benign Errors	1.0	1.2	0.7	0.8	0.8
Erroneous Readings	1.1	1.0	2.2	1.8	1.9

Table 6c groups the difference between glucose results from the FreeStyle Navigator system and the YSI into different blocks (within 20%, within 30% and within 40% from the YSI). It shows there is little change in the difference from YSI over time, thus demonstrating sensor stability.

Table 6c. Difference from the YSI at different times after sensor insertion

Time After Insertion (hours)	Percent Readings Within 20% of the YSI*	Percent Readings Within 30% of the YSI*	Percent Readings Within 40% of the YSI*
10-12	86	92	96
12-24	82	93	97
24-72	81	92	97
72-122	82	93	97

*The absolute difference from the YSI reading is measured in mg/dL if the YSI reading is at or below 75 mg/dL.

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Stability of Sensor Calibration

FreeStyle Navigator system typically requires a calibration at 10, 12, 24 and 72 hours after insertion of the sensor. This section presents information about the performance of the system by the 4 calibration periods. The table (Table 6d) breaks each calibration period into smaller slots and summarizes the difference from YSI in each slot. The data below demonstrates that there is little change in the system performance within each period.

Table 6d. Distribution of the difference from the YSI in the different calibration windows

Calibration Period		Percent Readings Within 20%* of the YSI	Percent Readings Within 30%* of the YSI	Percent Readings Within 40%* of the YSI
Cal 1 (typically occurs 10 hrs after sensor insertion)	First Calibration Period	80	88	94
Cal 2 (typically occurs 12 hours after sensor insertion)	First Third of Second Calibration Period	83	94	98
	Second Third of Second Calibration Period	83	94	98
	Final Third of Second Calibration Period	84	95	98
Cal 3 (typically occurs 24 hours after sensor insertion)	First Third of Third Calibration Period	84	94	98
	Second Third of Third Calibration Period	80	92	97
	Final Third of Third Calibration Period	80	91	95
Cal 4 (typically occurs 72 hours after sensor insertion)	First Quarter of Final Calibration Period	86	93	96
	Second Quarter of Final Calibration Period	84	92	96
	Third Quarter of Final Calibration Period	80	93	98
	Final Quarter of Final Calibration Period	82	93	97

* The absolute difference from the YSI reading is measured in mg/dL if the YSI reading is at or below 75 mg/dL.

Sample Glucose Traces

The following figures show examples of glucose traces from the In-Clinic study. These traces are representative examples of excellent, average and poor performance of the system. These traces show an overlay of the continuous glucose readings from the FreeStyle Navigator system and the blood glucose measurements made using the laboratory YSI reference. The blood glucose measurements that were used to calibrate the system are marked with 'x' in the traces. Glucose results from the FreeStyle Navigator system are shown using circles and the glucose results from the laboratory reference (YSI) are shown using triangles. Time (hours since sensor insertion) is on the horizontal axis, and glucose value in mg/dL is on the vertical axis.

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Figure 2. Sample of a Representative 'Excellent' Glucose Trace

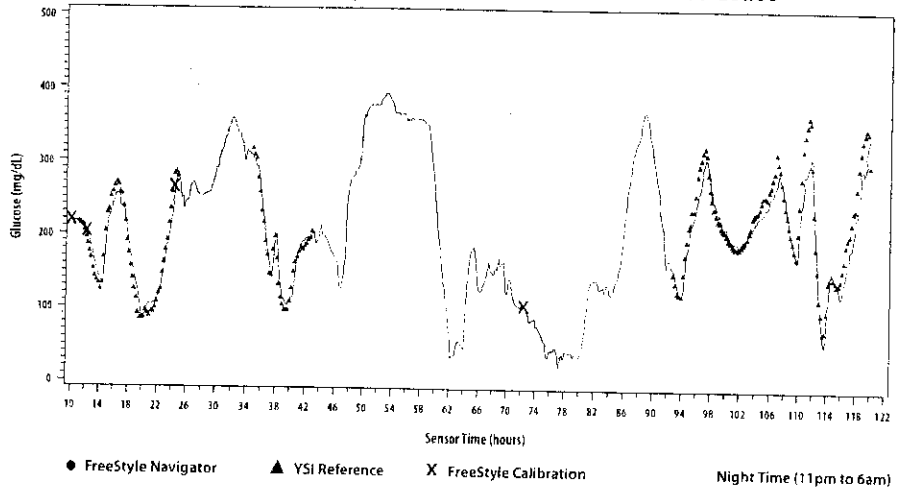


Figure 3. Sample of a Representative 'Average' Glucose Trace

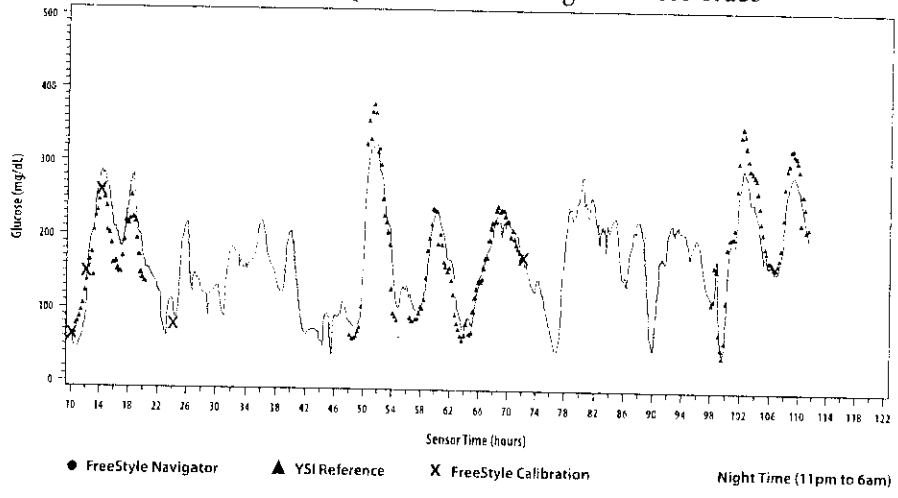
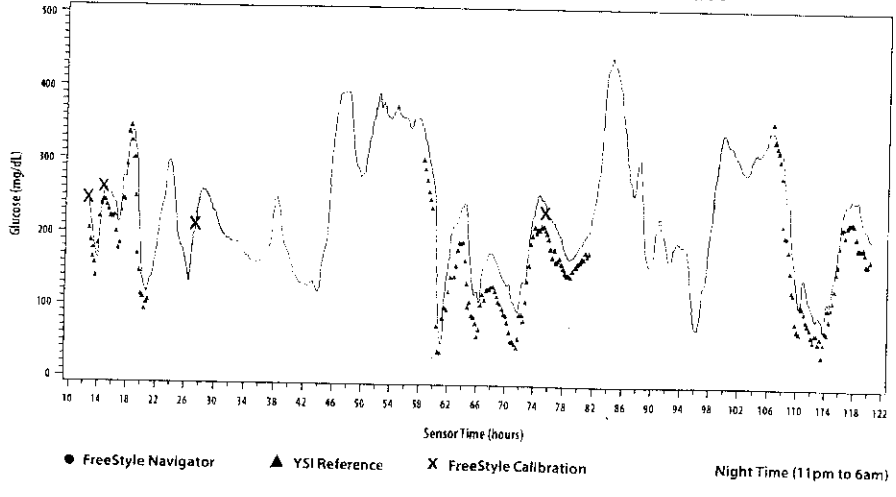


Figure 4. Sample of a Representative 'Poor' Glucose Trace



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Determination of Alarm Performance

The threshold alarm is characterized belowhere. The projected alarm performance has not been established.

The performance of low and high glucose alarms was assessed in an in-clinic study using 58 subjects with type 1 diabetes wearing one FreeStyle Navigator sensor on the arm and one sensor on the abdomen. FreeStyle Navigator continuous data were masked from the subjects and investigators and the alarms were not turned on. During 50 hours the subjects' venous glucose was tested with a YSI 2300 Stat Plus glucose analyzer at 15 minute intervals. Arm and abdomen data were pooled in the alarm analysis. Alarm performance was evaluated in a retrospective analysis of the study data. As alarm performance was developed retrospectively, your results may vary from those reported below.

Definitions:

Hypoglycemic event – two or more successive YSI measurements below the alarm threshold or one YSI measurement 6 mg/dL below the alarm threshold.

Hyperglycemic event - two or more successive YSI measurements above the alarm threshold or one YSI measurement 6% above the alarm threshold.

True Threshold Alarm - a threshold alarm that occurred ± 30 minutes from the start of a hypoglycemic or hyperglycemic event

True Alarm Rate – the percentage of time the glucose level was beyond the threshold and an alarm was activated

$$\frac{\text{Events Detected by True Threshold Alarms}}{\text{Total Events}} \times 100$$

Missed Alarm Rate -- the percentage of time the glucose level was beyond the threshold and an alarm was not activated

$$\frac{\text{Events Not Detected By True Threshold Alarms}}{\text{Total Events}} \times 100$$

False Threshold Alarm - a threshold alarm that occurred when a YSI measurement within ± 30 minutes was not beyond the threshold setting

False Alarm Rate – the percentage of time an alarm occurred when glucose level was not beyond the threshold setting

$$\frac{\text{False Threshold Alarms}}{\text{Total Threshold Alarms}} \times 100$$

Detection of Low Glucose

See Table 7 below for detection of low glucose. As an example, when the threshold alarm was set at 70 mg/dL (during the day), 56 % of the low glucose events were detected by FreeStyle Navigator.

Table 7 Low Glucose Detection

	DAY			NIGHT		
Low Alarm Setting (mg/dL)	**Day True Alarms***	**Day Missed Alarms****	**Day False Alarms*****	**Night True Alarms***	**Night Missed Alarms****	**Night False Alarms*****
	% (n/N†)	**% (n/N)**	**% (n/N)**	**% (n/N)**	**% (n/N)**	**% (n/N)**
65	46 (56/121)	54 (65/121)	19 (18/95)	80 (12/15)	20 (3/15)	41 (11/27)
70	56 (98/176)	44 (78/176)	16 (21/132)	79 (19/24)	21 (5/24)	40 (14/35)
75	59 (130/219)	41 (89/219)	9 (15/161)	72 (23/32)	28 (9/32)	37 (14/38)
85	61 (189/308)	39 (119/308)	7 (17/228)	65 (22/34)	35 (12/34)	33 (14/43)

* True Alarms are the percentage of time the glucose level was below the threshold and an alarm was activated
**Missed Alarms are the percentage of time the glucose level was below the threshold and an alarm was not activated.
***False Alarms are the percentage of time an alarm occurred but the glucose level was not below the threshold setting.
†n/N is the (n)umber of observations divided by the total (N)umber

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Detection of High Glucose

See Table 8 for detection of high glucose. As an example, when the threshold alarm was set at 240 mg/dL (during the day), 78 % of the high glucose events were detected by FreeStyle Navigator.

Table 8 High Glucose Detection

	DAY			NIGHT		
High Alarm Setting (mg/dL	Day True Alarms*	Day Missed Alarms**	Day False Alarms*	Night True Alarms**	Night Missed Alarms***	Night False Alarms***
	% (n/N†)	% (n/N)	% (n/N)	% (n/N)	% (n/N)	% (n/N)
180	89 (561/630)	11 (69/630)	11 (68/628)	69 (29/42)	31 (13/42)	7 (3/44)
240	78 (295/376)	22 (81/376)	12 (47/393)	41 (12/29)	59 (17/29)	25 (7/28)
270	70 (193/274)	30 (81/274)	12 (32/265)	21 (3/14)	79 (11/14)	36 (5/14)
300	61 (117/192)	39 (75/192)	12 (20/161)	12 (1/8)	88 (7/8)	33 (1/3)

* True Alarms are the percentage of time the glucose level was above the threshold and an alarm was activated
**Missed Alarms are the percentage of time the glucose level was above the threshold and an alarm was not activated.
***False Alarms are the percentage of time an alarm occurred but the glucose level was not above the threshold setting
†n/N is the (n)umber of observations divided by the total (N)umber

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Measuring Glucose in Interstitial Fluid

FreeStyle Navigator system measures glucose in the interstitial fluid (ISF) by means of a sensor that is inserted about 5 mm under the skin. Interstitial fluid is the fluid between the body's cells. Physiologic differences between the interstitial fluid and capillary blood may result in differences in glucose measurements. Differences in glucose measurement between interstitial fluid and your finger may be observed during times of rapid change in blood glucose, e.g. after eating, dosing insulin, or exercising. Movement of nutrients, oxygen and glucose from the blood into the cells happen across the ISF.

Therefore, if the glucose in the bloodstream rises (e.g. during meals), that rise is not seen in the ISF until later. Similarly, if glucose levels in the ISF drop (for example during exercise, the cells consume glucose rapidly) that drop is not seen in the bloodstream until later.

On average, glucose levels in the ISF lag the glucose levels in capillary blood by 14 minutes. This is a physiological phenomenon that can vary from one person to another.

Precision

Data from two sensors inserted at different insertion sites was used to calculate the between sensor reproducibility. Based on 312953 pairs of data sets, the average between sensor reproducibility was 10%.

Sensor Insertion, Calibration and Sensor Wear

Home Use Study: Sensor insertion, calibration and sensor wear were evaluated in a Home Use Study where 137 participants used the product on their own in a home environment. The participants wore 8 sensors during the study period of 40 days. They wore the sensors either on the arm or abdomen. During the first 20 days of the study, continuous glucose results were not visible to the participants. During the following 20 days, participants had access to the glucose measurements. In addition to required calibration tests, the participants performed 4 finger stick measurements a day using the built-in FreeStyle meter. The following information is based on the findings from this study.

When used as directed, 96.8% of the total sensor insertions were successful. 92.6% of the sensors were calibrated successfully and began producing glucose results within 12 hours after sensor insertion. The median time for a successful first calibration was 10.1 hours. The median duration of wear of calibrated sensors was 120 hours. 83% of sensor wears lasted at least 108.3 hours. The median wear time for sensors inserted on the arm was 0.4 hours longer than for sensors inserted on the abdomen.

Skin Interaction

Based on the examination of 124 study participants at a 21-day follow up, the following incidence of skin issues were observed in 304 site exams.
Moderate to severe itching – 1.6% of the time
Moderate bruising – 0.3% of the time
Moderate erythema – 1.0% of the time
Moderate pain – 0.3% of the time
Rate of mild incidences for any individual category of skin issues above including edema, rash, induration, bleeding and others was less than 5%.